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08/934,367

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTY. DOCKET NO.
08/934,367	09/19/97	NEEDLEMAN	~~F MCIN 103.0 (6~~

EXAMINER

HM21/1221

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ART UNIT	PAPER NUMBER
~~SCHEINER, T~~ 1642	9

DATE MAILED: 12/21/98

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

~~Responsive to communication(s) filed on~~ 12/7/98.

This action is **FINAL.**

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

ıortened statutory period for response to this action is set to expire 3 month(s), or thirty days, :hever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 16(a).

position of Claims

Claim(s) 1 - 21 is/are pending in the application.
Of the above, claim(s) _____ is/are withdrawn from consideration.
Claim(s) _____ is/are allowed.
Claim(s) 1 - 21 is/are rejected.
Claim(s) _____ is/are objected to.
Claim(s) _____ are subject to restriction or election requirement.

ılication Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
The drawing(s) filed on _____ is/are objected to by the Examiner.
The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
The specification is objected to by the Examiner.
The oath or declaration is objected to by the Examiner.

ırity under 35 U.S.C. § 119

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

] All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

Certified copies not received: _____.

Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

ıchment(s)

Notice of Reference Cited, PTO-892
Information Disclosure Statement(s), PTO-1449, ~~Paper No(s).~~ 3 sheets
Interview Summary, PTO-413
Notice of Draftperson's Patent Drawing Review, PTO-948
Notice of Informal Patent Application, PTO-152

DETAILED ACTION

Applicants traversal of the restriction has been considered, and Groups I and II have been rejoined. Claims 1-21 are pending in the application.

Information Disclosure Statement

SBIR Grant # R43 HL57045-01A1 (reference B29) has been considered, but its citation has been lined through on the 1449 submitted April 6, 1998 because it is not a publication.

Claim Rejections - 35 USC § 103

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rittershaus *et al.* (WO 9634888, published November 7, 1996) in view of Felgner *et al.* (U.S.P.N. 5,580,859), and further in view of Swenson et al. (Journal of Biological Chemistry, vol. 264, no. 24, pages 14318-14326, August 25 1989).

Claims 1-16 are directed to methods of increasing the concentration of HDL cholesterol in the blood of a mammal by eliciting antibodies that bind cholesterol ester transfer protein (CETP) and lessen the transfer of cholesterol esters from HDL (CETP); the methods comprise immunizing the mammal (whose blood already contains CETP) with recombinant DNA encoding either human or rabbit CETP, or with recombinant DNA encoding a fusion protein encoding an exogenous antigenic carrier (for example HBcAG) peptide-bonded to a CETP peptide (in one embodiment the CETP portion of the fusion protein has the amino acid sequence of either SEQ ID NO: 29 or 50). SEQ ID NO: 29 represents the 26 C-terminal amino acids of human CETP, while SEQ ID NO: 50 represents the 26 C-terminal amino acids of rabbit CETP. Claims 17-21 are directed to the DNA vaccines *per se*.

Rittershaus *et al.* disclose a method of increasing the concentration of HDL cholesterol in the blood of a mammal by eliciting antibodies that bind cholesterol ester transfer protein (CETP) and lessen the transfer of cholesterol esters from HDL (CETP); the method comprises inoculating the mammal with an isolated recombinant peptide vaccine comprising a broad range helper T cell epitope and a B cell epitope of CETP. Rittershaus *et al.*'s helper T cell epitope is an "exogenous

antigenic carrier." Moreover, the T and B cell epitopes are joined by a peptide bond. The reference also discloses using the vaccine to elicit anti-CETP antibodies in a host whose blood contains CETP, thereby increasing the concentration of HDL cholesterol in circulation. Rittershaus *et al.* differ from the instant invention in not disclosing inoculating with recombinant DNA to produce the ultimate peptide immunogen *in vivo*.

Felgner *et al.* are cited to show that there are several recognized advantages to eliciting peptide specific antibodies by direct administration of exogenous DNA (which are then expressed), rather than by administration of the peptide itself. Advantages include avoidance of anaphylactic reaction, sustained exposure, etc. It would have been obvious for one of ordinary skill in the art to have elicited CETP-specific antibodies by administering DNA encoding Rittershaus *et al.*'s peptide immunogens, rather then the peptide immunogens themselves, for the recognized advantages of direct DNA administration.

With respect to claim 15, Rittershaus *et al.* disclose immunogens wherein the CETP portion of the immunogen has the amino acid sequence of the 16 C-terminal amino acids of CETP (i.e., the last 16 CETP amino acids of the instant 26-amino acid immunogens) but differ from the instant invention in not specifying that the CETP portion of the vaccine molecules have the instantly recited 26-amino acid sequences.

Swenson *et al.* disclose inhibition of CETP transfer activity by a monoclonal antibody specific for a C-terminal epitope comprising the neutral lipid binding site on CETP. Swenson *et al.* do not name the individual amino acids of the instant sequences, but they explicitly refer to the

exact same region of the molecule represented by the instantly recited sequences, stating that "a monoclonal antibody (TP2) was obtained which neutralizes the cholesterol ester (CE) and triglyceride transfer (TG) activities of the CETP . . . the epitope of the inhibitory monoclonal antibody has been localized to a hydrophobic **26-amino acid sequence at the COOH terminus of CETP**" (emphasis added). This site corresponds exactly to the instantly specified portion of CETP. It would have been obvious for one of ordinary skill in the art to have selected those areas of CETP known to be involved in the transfer of cholesterol esters from HDL to use as an immunogen in Rittershaus *et al.*'s method, because one would have expected the antibodies elicited by the host to inhibit CETP transfer activity just as Swenson *et al.*'s did.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Toni R. Scheiner whose telephone number is (703) 308-3983. The examiner can normally be reached Monday-Friday from 8:30 to 5:00.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

12/18/98

Toni R. Scheiner

TONI R. SCHEINER
PRIMARY EXAMINER
GROUP 1600